

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED / ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		<small>ATTORNEY'S DOCKET NUMBER</small> P66606US0
INTERNATIONAL APPLICATION NO PCT/DK99/00589	INTERNATIONAL FILING DATE 29 October 1999	US APPLICATION NO (If known, see 7 CFR 1.5) 09/830666
TITLE OF INVENTION A METHOD TO CONTROL AN OVERACTIVE BLADDER		
APPLICANT(S) FOR DO/EO/US Nico J.M. RIJKHOFF, Thomas SINKJAER, Saso JEZERNIK -and- Warren GRILL		

Applicant herein submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information.

1. This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. A proper Demand for Internat'l. Preliminary Examination was made by the 19th month from earliest claimed priority date.
5. A copy of the International Application as filed (35 U.S.C. 371(c)(2))
 - a. is transmitted herewith (required only if not transmitted by the International Bureau).
 - b. has been transmitted by the International Bureau.
 - c. is not required, as the application was filed in the United States Receiving Office (RO/US)
6. A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
 - a. are transmitted herewith (required only if not transmitted by the International Bureau).
 - b. have been transmitted by the International Bureau.
 - c. have not been made; however, the time limit for making such amendments has NOT expired.
 - d. have not been made and will not be made.
8. A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. A translation of the annexes to the Internat'l. Preliminary Examination report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. An assignment document for recording. A separate cover sheet compliance with 37 CFR 3.28 and 3.31 is included.
13. A **FIRST** preliminary amendment.
 - A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. A substitute specification.
15. A change of power of attorney and/or address letter.
16. Other items or information:

International Search Report — Swedish Patent Office
 PCT Request Form
 PCT/IB/301 Form
 PCT/IB/308 Form
 First Page of Publication
 International Preliminary Examination Report — with Annexes (Article 19 Amendments)

US APPLICATION NO.(If known, see 37 CFR 1.5) 09/830666	INTERNATIONAL APPLICATION NO PCT/DK99/00589	ATTORNEY'S DOCKET NUMBER P66606US0		
17. <input checked="" type="checkbox"/> The following fees are submitted:		CALCULATIONS PTO USE ONLY		
Basic National Fee (37 CFR 1.492(a)(1)-(5)):				
Internat'l. prelim. examination fee paid to USPTO (37 CFR 1.492 (a) (1)) . . . \$690.00				
No international preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (2)) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) . . . \$710.00				
Neither international preliminary examination fee (37 CFR 1.492 (a) (3)) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO) \$1000.00				
International preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (4)) and all claims satisfied provisions of PCT Article 33(2)-(4) \$100.00				
Search Report prepared by the EPO or JPO (37 CFR 1.492 (a) (5)) \$860.00				
ENTER APPROPRIATE BASIC FEE AMOUNT =		\$ 1000.00		
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		\$ 130.00		
Claims	Number Filed	Number Extra	Rate	
Total Claims	18 - 20 =	-0-	x \$18.00	\$
Independent Claims	3 - 3 =	-0-	x \$80.00	\$
Multiple Dependent Claim(s) (if applicable)			+ \$270.00	\$
TOTAL OF ABOVE CALCULATIONS =		\$ 1130.00		
Reduction by 1/2 for filing by small entity , if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).		\$		
SUBTOTAL =		\$ 1130.00		
Processing fee of \$130 for furnishing the English translation later than <input type="checkbox"/> 20 <input checked="" type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f))		\$		
TOTAL NATIONAL FEE =		\$ 1130.00		
Fee of \$40.00 for recording the enclosed assignment (37 CFR 1.21(h)). Assignment must be accompanied by appropriate cover sheet (37 CFR 3.28, 3.31).		\$		
TOTAL FEES ENCLOSED =		\$ 1130.00		
		Amt. to be refunded: \$		
		Amt. charged: \$		
<p>a. <input checked="" type="checkbox"/> A check in the amount of \$ <u>1130.00</u> to cover the above fees is enclosed.</p> <p>b. <input type="checkbox"/> Please charge my Deposit Account No. <u>06-1358</u> in the amount of \$ <u> </u> to cover the above fees. A duplicate copy of this sheet is enclosed.</p> <p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge my account any additional fees set forth in §1.492 during the pendency of this application, or credit any overpayment to Deposit Account No. <u>06-1358</u>. A duplicate copy of this sheet is enclosed.</p>				
<p>SEND ALL CORRESPONDENCE TO: Jacobson, Price, Holman & Stern, PLLC 400 7th Street, N.W., Suite 600 Washington, DC 20004 202-638-6666</p> <p>CUSTOMER NUMBER: 00136</p>				
<p>By <u>Harvey B. Jacobson, Jr.</u> Harvey B. Jacobson, Jr. Reg. No. 20,851</p>				
JPH&S 3/95				

09/830666

JCDS Rec'd PCT/PTO 30 APR 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Nico J.M. RIJKHOFF et al.

Serial No.: New

Filing Date: April 30, 2001

For: A METHOD TO CONTROL AN OVERACTIVE BLADDER

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

IN THE CLAIMS

Please CANCEL amended claims 1-21. Please replace canceled claims with new claims 22-39 as found on the attached four sheets.

REMARKS

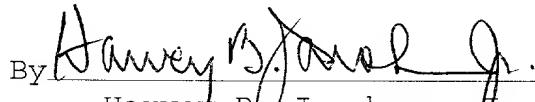
The foregoing Preliminary Amendment is requested in order to delete the multiple dependent claims and avoid paying the multiple dependent claims fee.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Early action on the merits is respectfully requested.

Respectfully submitted,

JACOBSON, PRICE, HOLMAN & STERN, PLLC

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Atty. Docket: P66606US0
Date: April 30, 2001
HBJ:jrc

Claims:

5 22. A method for controlling an overactive bladder, comprising the steps:

- detecting nerve signals from nerves innervating the bladder;
- detecting a bladder event from the nerve signals;
- generating electrical pulses in response to the detected event;
- stimulating afferent nerves using the generated electrical pulses in order to inhibit detrusor contraction of the bladder.

10 23. A method as defined in claim 22, wherein the detected nerve signals primarily come from afferents innervating mechanoreceptors in the bladder wall.

15 24. A method as defined in claim 22, wherein the detected nerve signals come from efferent nerve fibres innervating the bladder.

20 25. A method as defined in claim 22, wherein two different signals are used to detect a detrusor contraction, the first signals coming from afferent nerves innervating the bladder, and the second signals coming from efferent nerves innervating the detrusor muscle.

25 26. A method as defined in claim 22, wherein neural circuits inhibiting bladder contraction are stimulated by activating an inhibitory spinal reflex

by stimulating afferent nerve fibres innervating mechano-receptors located in the glans of the penis or clitoris.

27. A method as defined in claim 26, wherein a stimulation electrode is located at a nerve belonging to the group consisting of a dorsal penile/clitoris nerve, a pudendal nerve, an extradural sacral nerve root or an intradural dorsal sacral nerve root.

10 28. A method as defined in claim 22, wherein both a detecting electrode and a stimulation electrode is located at either the intradural dorsal sacral nerve roots or the extradural sacral nerve root.

15 29. A method as defined in claim 28, wherein the dorsal sacral nerve roots belong to the group S2-S4.

30. A method to estimate bladder volume, comprising the steps:

20 - detecting nerve signals from nerves innervating the bladder;
- estimate bladder volume in response to the detected signals using signal-processing methods.

25 31. A method as defined in claim 30, wherein the bladder volume is estimated from the amplitude of the detected nerve signal.

32. A method as defined in claim 30, wherein the bladder volume is estimated from the time between two detected nerve signals derived from two consecutive detrusor contractions.

33. A method as defined in claim 30 wherein the bladder volume is estimated from both the amplitude of the detected nerve signal and from the time between two detected nerve signals derived from two consecutive detrusor contractions.

34. A method as defined in claim 30, comprising the further steps of: transmitting, from a transmitter placed inside the body of a user, a signal when a predetermined threshold is exceeded, receiving the signal with a receiver placed outside the body of a user, actuating an alert in response to the received signal for alerting the user that a given threshold value for the bladder volume has been reached.

15

35. An apparatus for estimating bladder volume, comprising:

- sensor means for sensing nerve signals from nerves innervating the bladder;
- a unit capable of estimating bladder volume in response to the detected signals using signal-processing methods.

25 36. A apparatus as defined in claim 35, wherein the unit is capable of deriving a bladder volume from the amplitude of the detected nerve signal.

37. A apparatus as defined in claim 35, wherein the unit is capable of deriving a bladder volume from the 30 time between two detected nerve signals derived from two consecutive detrusor contractions.

38. A apparatus as defined in claim 35, wherein the unit is capable of deriving a bladder volume from both the amplitude of the detected nerve signal and from the time between two detected nerve signals derived from two consecutive detrusor contractions.

39. A apparatus as defined in claim 35, further comprising transmitting means, receiving means and actuating means,

- 10 - said transmitting means together with the unit being capable of being placed inside the body of a user;
- said receiving means, when placed outside the body of a user, being capable of receiving a signal from said transmitting means, when placed inside the body of a user, and passing the signal to actuating means for alerting the user that a given threshold value for the bladder volume has been reached.

A method to control an overactive bladder.

This application concerns a method to control an overactive bladder and to estimate bladder volume, comprising
5 an implanted sensor, which sensor comprises at least one nerve electrode to sense electrical signals, means for stimulation of nerves to inhibit detrusor contraction, an electronic unit to detect events from nerve signals and generate electrical pulses for stimulating nerves.

10

US 4,406,228 discloses a system that purportedly conditions pelvic floor musculature by means of neurostimulation for the purpose of controlling urinary loss. Such system includes stimulation apparatus for applying electrical pulses to electrodes implanted in the abdominal region or to a plug positioned in an anus. The plug contacts the sphincter muscle of the anus for the alleged purpose of inhibiting bladder contraction in response to excitation of the plug.

15

In this way the bladder volume is not measured, which can lead to bladder over distensions, and can lead to bladder rupture.

20

The storage phase of the micturition cycle requires a stable bladder with high compliance (i.e. a relaxed bladder) and closed urethral outlet. However, due to the feedback system the bladder may easily become unstable. Any stimulus that elicits a small burst of impulses in
25 the mechanoreceptor afferents, such as coughing and jumping may trigger an involuntary micturition reflex and cause urine leakage. To prevent this from happening the neural control system is equipped with several inhibitory circuits, both at spinal and supraspinal levels, which
30 prevent the detrusor muscle to contract. However, these inhibitory circuits are susceptible to a variety of neu-

rologic disorders. Therefore patients with neurologic disorders frequently suffer from urinary incontinence due to involuntary detrusor contractions.

- 5 The impaired storage function could in principle be improved by methods that decrease the sensitivity of the bladder afferents, decrease the activity of the bladder efferents or increase the bladder volume/capacity. Available treatment options are therefore: surgical augmentation of the bladder [Sidi et al., 1990], surgical deafferentation of the bladder [Koldewijn et al., 1994], the use of anticholinergic drugs and the use of intravesical capsaicin [Wiart et al., 1998].
- 10 15 Bladder inhibition by electrical stimulation has been described before [e.g. Vodušek et al., 1988; Wheeler et al., 1992] but only continuous stimulation was used, e.i. stimulation is permanent except during voiding.

20 **Ref**

Add: T. Lefurge, E. Goodall, K. Horch, L. Stensaas, and A. Schoenberg, "Chronically implanted intrafascicular recording electrodes," *Annals of Biomed. Eng.*, vol. 19, pp. 197-207, 25 1991.

Add: J.N. Sengupta, G.F. Gebhart, "Mechanosensitive properties of the pelvic nerve afferent fibres innervating the urinary bladder of the rat," *J. Neurophysiol.*, vol. 30 72, pp. 2420-2430, 1994.

The object of the inventions is:

- 1) treatment of involuntary loss of urine (incontinence)
35 due to involuntary detrusor contractions (detrusor overactivity)

2) estimation of bladder volume. This finds particular application in patients who use aids to empty their bladder e.g. intermittent catheterisation or electrical stimulation.

5

The invention finds particular application in patients where the involuntary detrusor contraction is associated with a neurologic disorder.

10 Treatment of detrusor overactivity and estimation of bladder volume can be achieved by a method as described in the first paragraph using a closed loop stimulation system to allow event driven inhibition of the bladder where stimulation is only applied when an undesired bladder contraction occurs, and an implanted sensor comprising at least one nerve electrode to sense electrical signals from nerves innervating the bladder. Sensing electrical signals related to mechanical bladder activity via said sensor, and detecting the onset of a bladder contraction, and estimation of bladder volume using signal processing methods, and activating an inhibitory neural circuit by stimulating afferent nerve fibres, in response to detection of the onset of a bladder contraction.

25

By this method no nerves have to be cut, and no irreversible surgery has to be done. Stimulation of neural tissue only takes place when needed, and the volume of the bladder is monitored. The present invention uses electrical stimulation to inhibit the bladder. Inhibition of the bladder by electrical stimulation is possible since, besides the mentioned neural inhibitory circuits, additional spinal inhibitory circuits exist to prevent involuntary leakage during e.g. defecation, coitus and physical activity. Activation of the afferent path of these neural circuits has two effects: they activate the in-

hibitory sympathetic neurones to the bladder and they provide central inhibition of the preganglionic detrusor-motoneurons through a direct route in the spinal cord. These additional inhibitory reflexes are not suppressed 5 during micturition, which means that they are quite capable of interrupting a detrusor contraction. Activation of these reflexes by electrical stimulation is a non-destructive alternative method for patients who are refractory to drugs, cannot tolerate the side effects or 10 for other reasons do not accept a drug treatment.

Primalarythe recorded nerve signals comes from afferents innervating mechanoreceptors located in the bladder wall. By detecting the onset of the bladder contraction the 15 stimulator could be activated only when contraction occurs, and continuos stimulation is not necessary. This minimises the risk of neural damages due to the stimulation. In addition, if the patient can sense the stimulation, the duration of stimulation should be minimised to 20 minimise the discomfort.

The step of implanting a sensor might comprise the step of implanting a nerve cuff electrode. The cuff electrode has been used successfully in other applications and has 25 been shown to be safe for human implants.

The step of implanting a sensor might comprise the step of implanting an intrafasicular electrode [Lefurge et al., 1991]. The intrafasicular electrode is flexible and 30 smaller, and might be preferred in locations where limited space is available.

The electrodes can be used to detect efferent or afferent nerve activity. The same electrode could be used to record both types of nerve signals. 35

The electrode can be placed on a nerve that contains afferent nerve fibres innervating mechanoreceptors located in the bladder. In this way information about the status
5 of the bladder can be obtained .

The electrode can be located at the intradural or extradural dorsal sacral nerve roots. In this way the electrodes can be placed at a mechanical stable position, and
10 the nerve roots are relatively long, which enables easy placement of electrodes.

The electrode can be placed on a nerve that contains efferent nerve fibres innervating the bladder, so bladder
15 activation can be monitored.

The electrode can be located at the intradural or extradural ventral sacral nerve roots. In this way the electrodes can be placed at a mechanical stable position,
20 and the nerve roots are relatively long, which enables easy placement of electrodes.

The electrode might be located at at least one of the preganglionic pelvic nerve branches and postganglionic
25 nerve branches. In this way nerve signals from the bladder can be recorded more selectively without contamination with signals from other organs.

Preferably two different nerve signals can be used to detect a detrusor contraction, where the first signal comes
30 from afferent nerves innervating the bladder, and the second signals comes from efferent nerves innervating the detrusor muscle. In this way the detrusor contraction can be detected more reliable.

Activating a neural circuit that inhibits the bladder contraction can be done by stimulating afferent nerve fibres, innervating mechanoreceptors, located in the glans of the penis or clitoris. In this way an ongoing detrusor 5 contraction can be aborted or stopped and leakage of urine will be prevented.

The bladder volume can be derived from the amplitude of the recorded afferent signal. By measuring of the bladder 10 volume the patient can be informed about his/her bladder volume.

The bladder volume can be derived from the time between 2 consecutive detrusor contractions. By measuring of the 15 bladder volume the patient can be informed about his/her bladder volume.

The bladder volume can be derived form both the amplitude of the recorded nerve signal and the time between 2 consecutive detrusor contractions. This way the bladder vol- 20 ume can be estimated in a more reliable way.

In the following the invention will be detailed described partly with reference to drawings.

25

Fig.1 shows a block diagram of event driven stimulation system to treat an overactive bladder.

Fig. 2 shows a block diagram of a bladder volume monitor- 30 ing system.

Fig. 3 shows schematically how the invention is applied.

Mechanoreceptors located in the bladder wall act as ten- 35 sion receptors and respond in graded fashion to increases in bladder volume and intravesical pressure [Sengupta and

Gebhart, 1994]. It has been shown that a close relationship between afferent nerve activity and the pattern of intravesical pressure changes is best observed when the activity of many afferent nerve fibres is summed. Sensor 5 14 comprises an implantable nerve cuff electrode. This type of electrode surrounds the selected nerve in close proximity so currents generated by the nerve fibres result in sufficient large voltage differences in the volume within the cuff so that they can be detected by the 10 electrode. However, other electrode configurations such as intrafasicular electrodes could also be used to detect the efferent nerve activity. The electrode needs to be placed on a peripheral nerve 15 that contains afferent 15 nerve fibres innervating mechanoreceptors located in the bladder. Possible locations for the electrode are therefore: intradural dorsal sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), preganglionic pelvic nerve branches and postganglionic nerve branches. An alternative method to detect a bladder contraction is to 20 record from the efferent nerve fibres that innervate the detrusor muscle. An increase in the efferent signal results in a detrusor contraction so an increased efferent signal indicates a detrusor contraction. Possible locations for the electrode to record efferent signals from 25 peripheral nerve 15 are: intradural ventral sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), preganglionic pelvic nerve branches and postganglionic nerve branches.

30 The output of the sensor 14 is passed through a circuit 13 that includes an amplifier and a filter. The output of circuit 13 is passed to circuit 10, which contains a detection algorithm that allows the detection of the onset of a sudden rise in intravesical pressure or a detrusor 35 contraction. The detection algorithm takes place in a signal processor 10, which will pass a trigger signal to

stimulator 11 when it detects such a pressure rise. The stimulator 11 includes one or more electrodes placed on peripheral sensory nerves 12. The stimulator 11 produces, in response to the trigger signal from circuit 10, an electrical potential difference, which will result in an electrical current through the electrode and adjacent nervous tissue. A rapid change in this electrical current activates or stimulates nerve fibres causing the production of action potentials in peripheral nerve 12. It has been shown that activation of afferent nerve fibres, innervating mechanoreceptors located in the glans of the penis or clitoris, has a strong inhibitory effect on the bladder. To obtain the desired effect of bladder inhibition upon stimulation the afferents should be stimulated somewhere along their course from mechanoreceptors to the sacral spinal cord. This means that possible locations for the electrode to be placed on peripheral nerve 12 are: dorsal penile/clitoris nerve, pudendal nerve, extradural sacral nerve roots (S2-S4) and intradural dorsal sacral nerve roots (S2-S4).

A system for monitoring the bladder volume is shown in FIG.2. Mechanoreceptors located in the bladder wall act as tension receptors and respond in graded fashion to increases in bladder volume and intravesical pressure. It has been shown that a close relationship exist between afferent nerve activity and bladder volume. In addition, bladder volume could be estimated from the time between two consecutive hyperreflexic bladder contractions since the number of contractions per time unit is proportional to the bladder volume. The preferred nerve electrode 25 for this purpose is an implantable nerve cuff electrode, although other electrode configurations could also be used. The sensor 25 comprises an electrode, which needs to be placed on a peripheral sensory nerve 26 that contains afferent nerve fibres innervating mechanoreceptors.

located in the bladder. Possible locations for the sensor 25 are therefore: intradural dorsal sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), pregan-glionic pelvic nerve branches and postganglionic nerve 5 branches. Sensor 25 could be the same one as sensor 14 so the systems of FIG.1 and FIG.2 share the same electrode.

The output of the sensor 25 is passed through a circuit 24 that includes an amplifier and a filter. The output of 10 circuit 24 is passed to signal processing unit 20, which contains an estimation algorithm that allows estimation of bladder volume. If the estimated volume exceeds the volume threshold then a trigger signal will be passed to transmitter 21. Upon receiving a trigger, transmitter 21 15 sends a signal to receiver 22 using radio waves. Receiver 22 is placed outside the body and will, upon receiving a signal from transmitter 21, pass a signal to actuator 23. Actuator 23 will alert the user that the bladder volume exceeded the volume threshold. Various devices could be 20 used as actuator such as a buzzer, a vibrator, etc.

Fig. 3 shows in detail the elements of the invention. A Bladder 31 with a closing mechanism comprising a sphincter 32 together with the innervating peripheral nerves, which comprises 34 intradural dorsal sacral root 34, intradural ventral sacral root 35, extradural sacral root 36, Preganglionic Pelvic nerve 37, Postganglionic pelvic nerve 38 and Pudendal nerve 39. In addition the dorsal penile/clitoral nerve 40 is shown. These nerves 25 relay information to and from the spinal cord 33. A recording electrode 41 senses information from the nerves 37, and electrical information is transmitted through an electrode lead 43 to a signal processing unit 44, which 30 is connected to a stimulator 45. Signal from stimulator 45 is transmitted through an electrode lead 43 to a stimulation electrode 42, which stimulates nerve 40. 35

- 10 Signal processor
- 11 Stimulator
- 12 Peripheral sensory nerve
- 5 13 Amplifier
- 14 Sensor
- 15 Peripheral nerve

- 20 Signal processor
- 10 21 Transmitter
- 22 Receiver
- 23 Actuator
- 24 Amplifier
- 25 Sensor
- 15 26 Peripheral sensory nerve

- 31 Bladder
- 32 Sphincter
- 33 Spinal cord
- 20 34 intradural dorsal sacral root
- 35 intradural ventral sacral root
- 36 extradural sacral root
- 37 Preganglionic Pelvic nerve
- 38 Postganglionic pelvic nerve
- 25 39 Pudendal nerve
- 40 Dorsal penile/clitoral nerve
- 41 Recording electrode
- 42 Stimulation Electrode
- 43 Electrode lead
- 30 44 Signal processing unit
- 45 Stimulator

Claims:

1. An apparatus for estimating bladder volume, comprising:

5

- sensor means for sensing nerve signals from nerves innervating the bladder;

10 - a unit capable of estimating bladder volume in response to the detected signals using signal-processing methods.

15 2. An apparatus as defined in claim 1, wherein the unit is capable of deriving a bladder volume from the amplitude of the detected nerve signal.

20

3. An apparatus as defined in claim 1, wherein the unit is capable of deriving a bladder volume from the time between two detected nerve signals derived from two consecutive detrusor contractions.

25

4. An apparatus as defined in claim 1, wherein the unit is capable of deriving a bladder volume from both the amplitude of the detected nerve signal and from the time between two detected nerve signals derived from two consecutive detrusor contractions.

30 5. An apparatus as defined in any of claims 1 to 4, further comprising transmitting means, receiving means and actuating means,

35

- said transmitting means together with the unit being capable of being placed inside the body of a user;

- said receiving means, when placed outside the body of a user, being capable of receiving a signal from said transmitting means, when placed inside the body of a user, and passing the signal to actuating means for
5 alerting the user that a given threshold value for the bladder volume has been reached.

6. A non-therapeutic method to estimate bladder volume, comprising the steps:

10

- detecting nerve signals from nerves innervating the bladder;

15

- estimate bladder volume in response to the detected signals using signal-processing methods.

7. A method as defined in claim 6, wherein the bladder volume is estimated from the amplitude of the detected nerve signal.

20

8. A method as defined in claim 6, wherein the bladder volume is estimated from the time between two detected nerve signals derived from two consecutive detrusor contractions.

25

9. A method as defined in claim 6, wherein the bladder volume is estimated from both the amplitude of the detected nerve signal and from the time between two detected nerve signals derived from two consecutive detrusor contractions.
30

10. A method as defined in any of claims 6 to 9,

comprising the further steps of: transmitting, from a transmitter placed inside the body of a user, a signal when a predetermined threshold is exceeded, receiving the signal with a receiver placed outside the body of a user,
5 actuating an alert in response to the received signal for alerting the user that a given threshold value for the bladder volume has been reached.

11. A method to estimate bladder volume, comprising
10 the steps:

- detecting nerve signals from nerves innervating the bladder;
- 15 - estimate bladder volume in response to the detected signals using signal-processing methods.
- 12. An apparatus for controlling an overactive bladder, comprising:
20
 - sensor means for sensing nerve signals from nerves innervating the bladder;
 - 25 - a unit capable of detecting a bladder event from the nerve signals, the unit being capable of generating a stimulating signal in response thereto; and
 - means for stimulation of nerves using the generated stimulating signal in order to inhibit detrusor contraction.
30
- 13. An apparatus as defined in claim 12, comprising

a single nerve electrode serving as both a sensor means and stimulation means, said nerve electrode being adapted to be implanted on either the intradural dorsal sacral nerve roots (S2-S4) or the extradural sacral nerve root
5 (S2-S4).

14. An apparatus as defined in claim 12 or 13, wherein said sensor means is capable of sensing two different nerve signals, and where the unit is capable of
10 detecting a bladder event from said two different nerve signals.

15. A method to control an overactive bladder, comprising the steps:

15 - detecting nerve signals from nerves innervating the bladder;

20 - detecting a bladder event from the nerve signals;

25 - generating electrical pulses in response to the detected event;

- stimulating afferent nerves using the generated electrical pulses in order to inhibit detrusor contraction of
25 the bladder.

16. A method as defined in claim 15, wherein the detected nerve signals primarily come from afferents inner-
30 vating mechanoreceptors in the bladder wall.

17. A method as defined in claim 15, wherein the de-

tected nerve signals come from efferent nerve fibres innervating the bladder.

18. A method as defined in claim 15, wherein two different signals are used to detect a detrusor contraction, the first signals coming from afferent nerves innervating the bladder, and the second signals coming from efferent nerves innervating the detrusor muscle.
- 10 19. A method as defined in any of claims 15 to 18, wherein neural circuits inhibiting bladder contraction are stimulated by activating an inhibitory spinal reflex by stimulating afferent nerve fibres innervating mechano-receptors located in the glans of the penis or clitoris.
- 15 20. A method as defined in claim 19, wherein a stimulation electrode is located at a dorsal penile/clitoris nerve, a pudendal nerve, a extradural sacral nerve root or an intradural dorsal sacral nerve root.
21. A method as defined in claim 15, wherein both a detecting electrode and a stimulation electrode is located at either the intradural dorsal sacral nerve roots (S2-S4) or the extradural sacral nerve root (S2-S4).

09/830666

Abstract

This application concerns a method to control an overactive bladder and to estimate bladder volume, comprising an implanted sensor, which sensor comprises at least one nerve electrode to sense electrical signals, means for stimulation of nerves to inhibit detrusor contraction, an electronic unit to detect events from nerve signals and generate electrical pulses for stimulating nerves. The object of the invention is treatment of involuntary loss of urine (incontinence) due to involuntary detrusor contractions (detrusor overactivity). Another object of the invention is estimation of bladder volume. This finds particular application in patients who use aids to empty their bladder e.g. intermittent catheterisation or electrical stimulation.

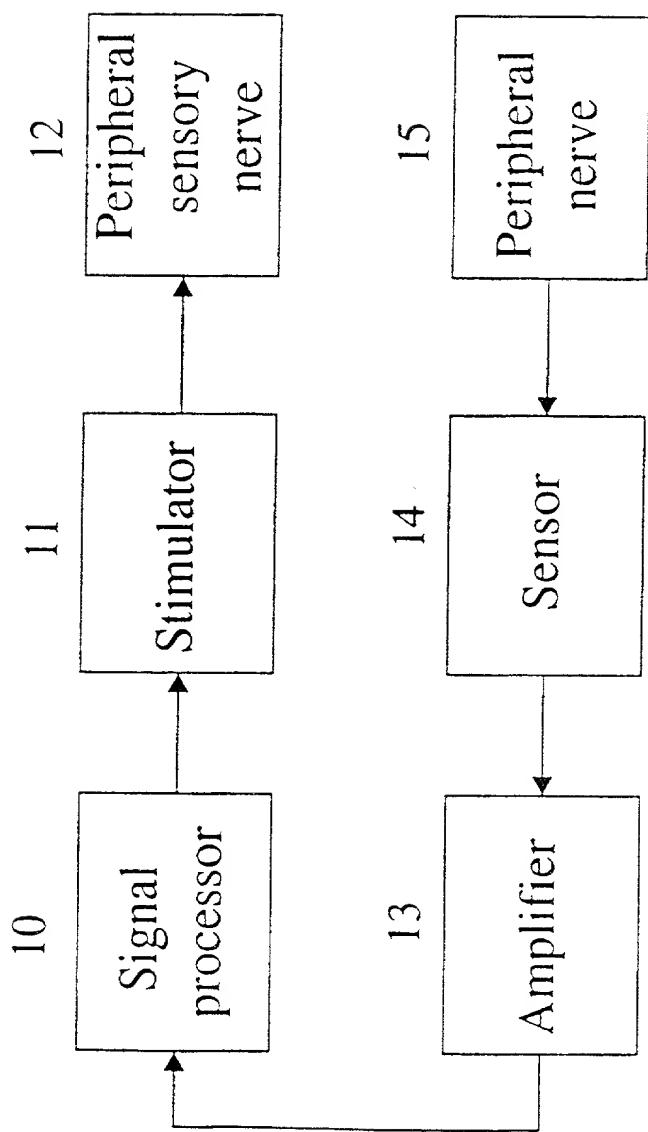


Fig. 1
Bladder patent

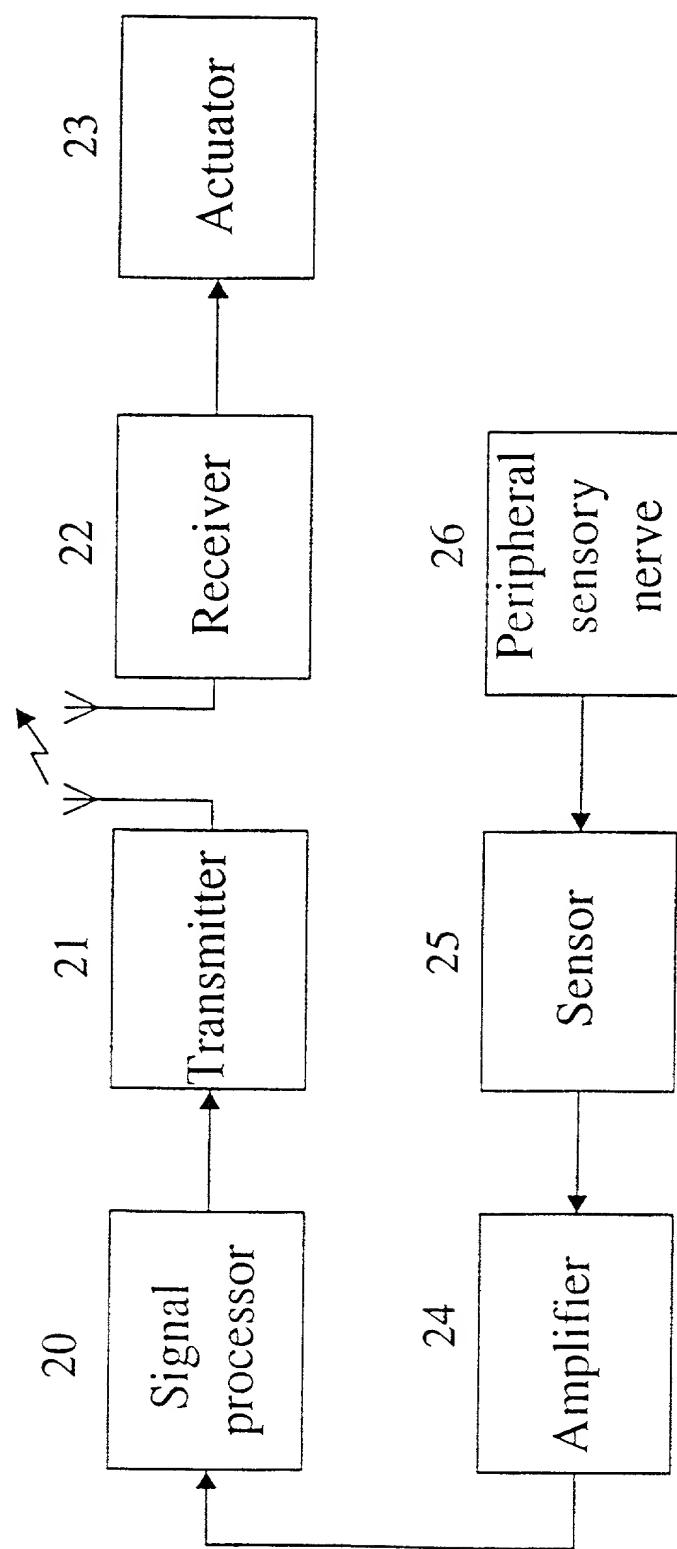


Fig. 2
Bladder patent



09/830666

PCT/DK99/00589

WO 00/25859

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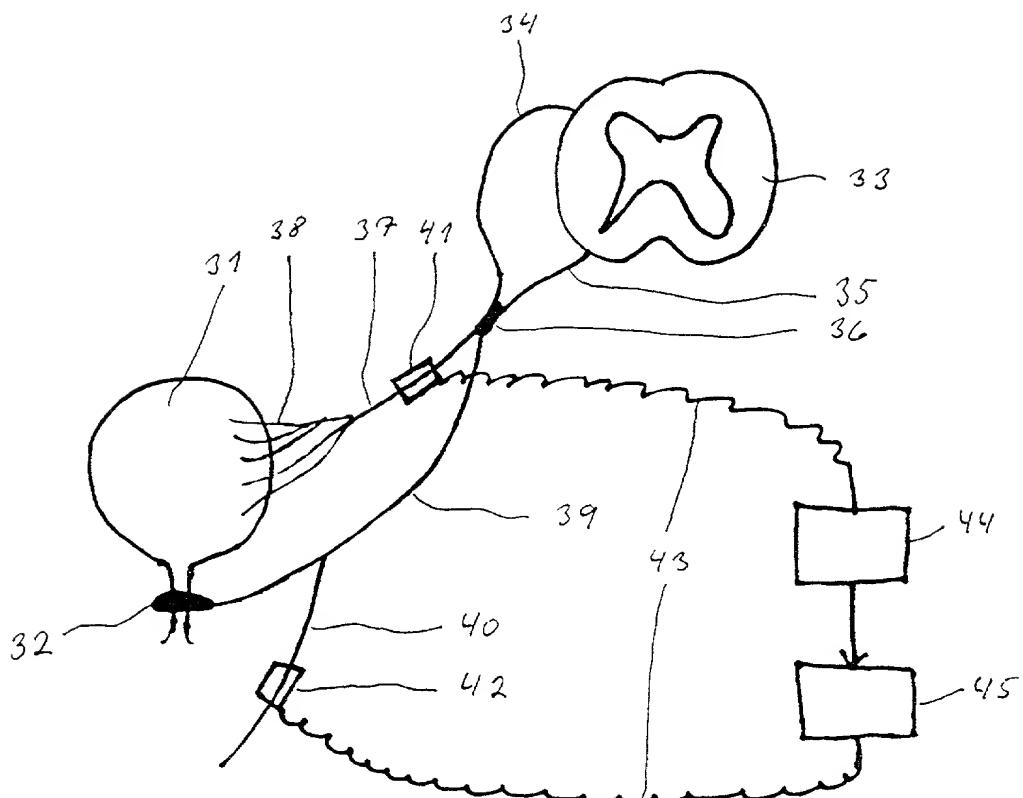


Fig. 3

**DECLARATION
AND POWER OF ATTORNEY
U.S.A.**

ALL PATENT'S, INCLUDING DESIGN
FOR APPLICATION BASED ON PCT; PARIS CONVENTION;
NON PRIORITY; OR PROVISIONAL APPLICATIONS

ATTORNEYS' USE ONLY
ATTORNEYS' DOCKET NO.

As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name, the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or an original, first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled

A method to control an overactive bladder

which is described and claimed in: PCT International Application No. PCT/DK99/00589 filed October 29, 1999
 the attached specification the specification in application Serial No. _____ filed _____
 (if applicable) and amended on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56

I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed
PA 1998 01396	Denmark	30.10.1998	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
(Number)	(Country)	(Day/Month/Year Filed)	<input type="checkbox"/> Yes <input type="checkbox"/> No
			<input type="checkbox"/> Yes <input type="checkbox"/> No

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing Date) (Status: patented, pending, abandoned)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorneys (Registration No.) to prosecute this application, receive and act on instructions from my agent, and transact all business in the Patent and Trademark Office connected therewith. HARVEY B. JACOBSON, JR. (20,851); D. DOUGLAS PRICE (24,514); JOHN CLARKE HOLMAN (22,769); MARVIN R. STERN (20,640); ALLEN S. MELSER (27,215); MICHAEL R. SLOBASKY (26,421); JONATHAN L. SCHERER (29,851); IRWIN M. AISENBERG (19,007); WILLIAM E. PLAYER (31,409); YOUNG S. HAM (45,307) and NATHANIEL A. HUMPHRIES (22,772)

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I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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DATE <u>24-04-2001</u>	DATE <u>24-04-2001</u>	DATE <u>02-05-2001 (May)</u>

Additional inventors are named on separately numbered sheets attached hereto.

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MAY 14, 2001
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